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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,634	03/23/2004	Manuel Fresno Escudero	A34909-PCT-USA-1 069277.0	2456
21003	7590	01/26/2005	EXAMINER PAK, YONG D	
BAKER & BOTTS 30 ROCKEFELLER PLAZA NEW YORK, NY 10112			ART UNIT 1652	PAPER NUMBER

DATE MAILED: 01/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application N .

10/806,634

Applicant(s)

FRESNO ESCUDERO ET AL.

Examin r

Yong D Pak

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1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 23 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 9-12 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 9-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 10/031,047.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 3/5/02.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

This application is a divisional of 10/031,047.

The preliminary amendment filed on March 23, 2004, canceling claims 1-8 and adding claims 9-12, has been entered.

Claims 9-12 are pending. Claims 9-12 are under consideration.

### ***Information Disclosure Statement***

The information disclosure statement (IDS) submitted on March 5, 2002 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

### ***Sequence Compliance***

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. In Figure 2, there are two nucleic sequences but only one sequence is identified by a sequence identification number in the specification. See particularly 37 CFR 1.821(d).

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 9 and claims 10-12 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 recites the phrase "measuring the reporter gene activity". It is unclear if the reporter gene activity is directly measured or if the activity of the encoded reporter protein is measured. If the reporter gene activity is measured, it is unclear how a gene's activity is directly measured. Examiner has interpreted the phrase as measuring the activity of the encoded reporter protein.

It is also not clear to the Examiner as to how those skilled in the art can conclude that the compound identified by the above method is indeed a transcriptional inhibitor of COX-2 and not a compound which binds to the stimulator (inducer) thereby preventing the induction of COX-2. This is because in step (a) of the assay, applicants contact the cell expressing COX-2, the inducer and the test compound all together. Applicants have not set up any control steps in which a direct interaction between the inducer and the test compound is prevented or if any controls steps are taken into consideration. Therefore, the method lacks essential step(s).

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 11, is it unclear what which "human promoter" applicants are referring to. It appears that applicant may have used the phrase to indicate that the COX-2 promoter

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is isolated from human. If that is so, amending the claim as "wherein the cyclooxygenase-2 promoter is isolated from human" would overcome the rejection.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "PMA" is unclear. It appears that applicant may have used it as a short form for phorbol myristate acetate. If that is so, reciting the full name of the compound would overcome the rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. (See rejection of claims 9-12 under 35 U.S.C. 112, 2<sup>nd</sup>)

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir., 1988). They include (1) the quantity of experimentation necessary, (2) the amount of

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direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to a method identifying compounds that inhibit transcription of a human COX-2 gene by contacting a human COX-2 promoter, stimulator (inducer) and a test compound all together, wherein inhibition of transcription is determined by measuring amount of the reporter protein activity in the cell. However, one of ordinary skill in the art cannot conclude that the compound identified in the claimed method is a transcriptional inhibitor of COX-2 and not a compound which binds to the inducer, thereby preventing the transcription of COX-2. (See rejection of claims 9-12 under 35 U.S.C. 112, 2<sup>nd</sup>).

The claims are not commensurate with the enablement provided by the disclosure with regard to uncertainty that a decrease or absence of the reporter protein activity in the cell is indicative of the test compounds being inhibitors of COX-2 transcription for the reasons discussed above. It would require undue experimentation of the skilled artisan to practice the claimed method. The specification provides no guidance with regard to differentiating test compounds that bind to the COX-2 promoter and inhibiting transcription of a COX-2 gene and test compounds that bind to the inducer. In view of the great breadth of the claim, amount of experimentation required to practice the claimed method, the lack of guidance, working examples, and unpredictability of the art in differentiating test compounds that bind to the COX-2

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promoter or the inducer, the claimed invention would require undue experimentation.

As such, the specification fails to teach one of ordinary skill how to practice the claimed method.

The specification does not support the claims which encompass a method of contacting the COX-2 promoter, inducer and test compound all together because the specification does not establish: (A) controls to determine direct interaction between the inducer and the test compound; (B) a rational and predictable scheme for testing any test compound with an expectation of obtaining a transcriptional inhibitor of COX-2 and not test compounds binding to the inducer; and (C) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to practice the claimed invention. Without sufficient guidance, determination of a method of identifying test compounds as transcriptional inhibitors of COX-2 is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

***Claim Rejections - 35 USC § 103***

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kutchera et al. and Dannenberg et al. (see rejection of claims 9-12 under 35 USC 112, 2<sup>nd</sup> paragraph for the interpretation of the phrase "measuring reporter gene activity").

Claims 9-12 are drawn to a method of identifying compounds that inhibit the induction of human cyclooxygenase-2 gene transcription by contacting a cell comprising 1.9 kb of a human COX-2 promoter linked to a luciferase gene with a test compound in the presence of a PMA and an ion, a stimulator of COX-2 gene.



Kutchera et al. (form PTO-892) teach a 1.9 kb of a human COX-2 promoter linked to a luciferase gene (abstract, page 4817, left column and page 4818, right column). Kutchera et al. also teach that the luciferase gene linked to the promoter region of human COX can be used to examine transcription levels of the COX gene (page 4818, right column).

The difference between the reference of Kutchera et al. and the instant invention is that the reference of Kutchra et al. does not teach the use of said construct for identifying compounds that inhibit the induction of human COX-2.

Dannenberg et al. (WO 98/37235 or U.S. Patent No. 6,200,760 – form PTO-1449) teach a method of identifying compounds that inhibit the induction of human cyclooxygenase-2 gene by contacting a cell comprising a human COX-2 promoter linked to a luciferase gene with a test compound in the presence of a PMA and an ion and measuring luciferase activity in the presence and absence of test compounds (pages 6-10, 14-17 and 23-25 or (abstract, Columns 2-8 and claims 1-2). However, the human COX-2 promoter of Dannenberg is 1.4 kb.

Therefore, combining the teachings of Kutchera et al. and Dannenberg et al., it would have been obvious to one having ordinary skill in the art to interchange the polynucleotide construct of Dannenberg et al. with the polynucleotide construct of Kutchera et al. in practicing the method of Dannenberg et al. One of ordinary skill in the art would have been motivated to combine the references in order to rapidly screen for inhibitors of COX-2 using the shorter fragment of Dannenberg et al. or the longer promoter fragment of Kutchera et al., which has the potential of binding more test

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compounds, thereby resulting in a more comprehensive assay of screening for transcriptional inhibitors of COX-2. One of ordinary skill in the art would have had a reasonable expectation of success since Kutchera et al. teaches that the luciferase gene linked to the COX-2 promoter can be used to monitor transcription levels and Dannenberg et al. successfully teaches a method of identifying compounds that inhibit induction of COX-2 by measuring luciferase activity, wherein the luciferase gene is ligated to a promoter of human COX-2.

Therefore, the above references render claims 9-12 prima facie obvious to one of ordinary skill in the art.


None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak  
Patent Examiner 1652

  
Manjunath Rao  
Primary Examiner 1652